Highlights of Scientific Summits Meeting

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SUMMARY

Since last year a board of respectively three urologists and one radiation oncologist created the 'Scientific Summits'. This is a scientifically independent Belgian congress for urologists, radiation oncologists, medical oncologists and radiologists with special interest in urology and more specifically in urologic oncology. The aim of Scientific Summits is providing up-to-date scientific information based on the highlights of the most recent international congresses. The 4th edition took place in the charming city of Durbuy, Belgium.

The first day of the meeting focussed on the treatment and prevention of side effects of various anticancer treatments in urologic oncology. Experts in the field shared practical tips and tricks, based on interactive case discussions. They illustrated difficult situations and how to deal with them. On the second day of the meeting, interactive state-of-the-art lectures provided us with up-to-date information on how to evaluate and manage advanced and recurrent prostate cancer.

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COPING WITH SIDE EFFECTS OF LOCAL TREATMENT OF PROSTATE CANCER

The overall gastrointestinal and genitourinary toxicity with modern radiotherapy is acceptable.[10] There is a moderate but mostly transient increase in toxicity when shorter radiotherapy regimens are applied (hypofractionation)[1,2]. Radiation-associated urethral strictures and stenoses are difficult to manage, primarily because of poor tissue vascularisation and proximity to the striated sphincter.[9] These patients can be managed endoscopically with dilation or incision of the stricture. However, the recurrence rate mounts to 50% within the first 16-60 months after treatment. Ten percent need permanent catheterisation and 10% are urinary incontinent. After EBRT and brachytherapy, respectively 1-13% and 2-12% of patients develop strictures.[3-5,8] A history of transurethral resection of the prostate (TURp) significantly increases the risk of developing urethral strictures.[8]

Incontinence due to radiotherapy or surgery, can be surgically treated with a male sling or an artificial urinary sphincter. The latter has similar results post-surgery and post-radiotherapy.[6] Male slings have inferior results after radiotherapy.

Other urinary side effects of radiotherapy are frequency, urgency or obstruction.[3,4,5,8] These can be medically treated with tamsulosin, NSAID or PDE5- inhibitors. Surgical treatment, however very rarely needed, includes TURp.

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COPING WITH SIDE EFFECTS OF SYSTEMIC TREATMENT OF PROSTATE, KIDNEY AND BLADDER CANCER

For metastatic hormone naïve prostate cancer, treatment remained roughly unchanged from 1941 until 2015. Since the results of the CHAARTED Trial became mature in 2015, treatment options were expanded in *de novo* metastatic cancer patients.[12] Particularly in high-volume metastatic disease, the addition of docetaxel to androgen deprivation therapy (ADT) increased overall survival by approximately twelve months, at the cost of more treatment induced toxicity.[12] Since then, several trials published their results in *de novo* metastatic prostate cancer (STAMPEDE, LATITUDE, PEACE-I Trial, MD Anderson US Trial).[14,15,20] All these trials demonstrated an overall survival benefit when a second anti-tumoral medication (docetaxel, abiraterone) was added to ADT with the largest advantage observed in high volume metastatic prostate cancer.[11,14,15,20]

A very interesting remark was made by Prof. Sautois, who showed data that chemotherapy-induced neutropenia acts as a surrogate for overall survival.[21,22] Dose-reduction of chemotherapy is always based on prevention or further avoidance of side-effects. Dose reduction might lead to lower response. Based on the available data, there was a very lively discussion based on the following question: "Should we offer every man with *de novo* locally advanced or metastatic hormone-sensitive prostate cancer docetaxel or abiraterone?". This discussion was moderated by Prof. Stranne, an expert in the field working at the University of Gothenburg, Sweden. Prof. Stranne raised an important remark concerning both the STAMPEDE and the LATITUDE trials.[14,15] In both trials, only 40% and 27% of the patients in the control group received the optimal treatment at time of progression, whatever the reason might have been.[14,15] He also critically mentioned that in these three studies, only healthy men with very high risk disease were included. "This is not the "Average Joe", as we see him at the daily clinic practice", Prof Stranne said. Indeed, we also need to calculate the impact of side effects of these new treatments. The most common ≥3 adverse side effect of docetaxel is neutropenia or febrile neutropenia (20%). In comparison, 15% of patients treated with abiraterone develop ≥3 adverse events, mostly related to mineralocorticoid excess (hypokalaemia, hypertension) and liver failure.

In conclusion, the panel agreed that adding docetaxel or abiraterone to ADT should be reserved for *de novo* metastatic patients with high-volume metastatic disease. The definition of high-volume is not straightforward, but can be defined as the presence of at least four metastatic lesions (M1a-M1b-M1c), hereby clearly excluding N1 disease. The latter is considered pelvic disease and should be treated with curative intent. This brought the discussion to the very important remark: we should not forget local treatment in N1M0 disease. The question whether local treatment is of benefit in M1 disease leads to a very open-minded discussion.

There are new treatment options for kidney and bladder cancer, the so-called 'new kids on the block': immune checkpoint inhibitors. In Belgium, recently, pembrolizumab and nivolumab have been reimbursed in the treatment armamentarium of bladder and kidney cancer respectively. Pembrolizumab is only reimbursed in specific cases when there is failure or intolerance for platinum. With these immune checkpoint inhibitors, we deal with other side effects, mainly auto-immune reactions. Usually they are mild but they occur frequently (>10%). Mainly the skin, gastro-intestinal and liver are affected within two months (early side effects), late side effects may occur in the lungs, kidney or endocrine system. The latter may happen even after finishing the treatment. Treatment includes topical treatment, systemic steroid or immunosuppressive drugs (TNF α inhibitors).

IMAGING OF PCA RELAPSE

Prof. Villeirs, expert in urological radiology at the Ghent University Hospital presented an overview on the imaging possibilities in patients with biochemical relapse after local treatment for prostate cancer. Local recurrence after radical prostatectomy is predominantly located in the perianastomotic and retrovesical area.[24,26,27] Whenever visible, the average diameter is 1,5 cm with a volume depending on the current PSA value.[25]

Nowadays, multiparametric magnetic resonance imaging (mpMRI) is widely accepted as the state-of-the-art imaging modality for local recurrence after radical prostatectomy. With T2-weighted MRI alone the rate specificity varies between 52-82% due to residual benign prostatic tissue, hyper intense scars, hematomas and seminal vesicle remnants.[28] Dynamic contrast-enhanced (DCE) MRI is able to differentiate between these benign abnormalities leading to an increase in specificity and sensitivity with increasing PSA level.Therefore, an mpMRI in the setting of suspected local recurrence after radical prostatectomy should always include DCE MRI.[22]

When a local relapse after radiotherapy is suspected, mpMRI is the best imaging modality to detect and confirm the local recurrence.[29] Also in this setting, DCE-MRI is the modality with the highest sensitivity and specificity, although there is accumulating evidence from the literature that present-day diffusion-weighted imaging (DWI) may show comparable results.[30]To conclude, an mpMRI with DCE and increasingly also DWI is the best choice for detecting local recurrence after radiotherapy. However, do not perform DCE immediately after radiotherapy and wait at least three months because

KEY MESSAGES FOR CLINICAL PRACTICE

1. **The overall gastrointestinal and genitourinary toxicity with radiotherapy is low and very acceptable due to the evolutionary techniques.**
2. **Check point inhibitors: Pembrolizumab has been approved as first-line treatment in bladder cancer whereas nivolumab in kidney cancer.**
3. **First-line treatment with docetaxel or abiraterone in combination with androgen deprivation only for high volume metastatic. We should not forget local treatment in locally-advanced high-risk disease.**
4. **Multiparametric MRI is the state-of-art imaging modality for local recurrence after radiotherapy or radical prostatectomy.**
5. **Upcoming disruptive healthcare system: complex and still a challenge.**

inflammatory reactions of the tissue may cause false positive enhancement due to an increase in perfusion.

The major question remains whether all this new biological imaging has an impact on treatment? To answer this question, Prof. Ost was invited to give a state-of-the-art lecture and add his own opinion. Prof. Ost is a radiation oncologist at the Ghent University Hospital and an expert in the field on metastatic prostate and kidney cancer. There were some important conclusions, directly applicable in daily clinical routine. At first, patients with a detectable PSA after radical prostatectomy should be referred for salvage RT especially if biological imaging (PMSA scan) is negative.[30] Nuclear scans (especially PSMA) will detect metastases earlier when compared to anatomical imaging. However, we should only perform these biological imaging scans if their results will impact on treatment decision. In this viewpoint, metastatic-directed treatment of oligometastatic disease is a beautiful example.

ETHICS AND ECONOMY

At the conclusion of the two day congress Dr. Ameye (Department of Urology, Maria-Middelares Hospital, Ghent) and Dr. Demeere (Department of Urology, Sint-Jan, Brussels) gave the latest updates about the upcoming new working system within the healthcare system. They concluded with an explanation about the low variable care which starts the 1st of September 2018: with attention to the correct planning of the intervention, perfect nomenclature number, correct ICD-10 to the only once principle technique.

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